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Ambulatory blood pressure in microalbuminuric type 1 diabetic patients

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Ambulatory blood pressure in microalbuminuric type 1 diabetic patients. Twenty-four-hour ambulatory blood pressure (AMBP) was performed in microalbuminuric (micro.) type 1 diabetic patients, with the aim of comparison with a matched group of normoalbuminuric patients (normo.) and healthy controls. Thirty-four patients without antihypertensive medication were investigated in each group. Urinary albumin excretion (UAE) for micro. was (geometric mean, tolerance factor μg/min) 51.7 ×/÷ 1.94, 5.1 ×/÷ 1.88 for normo. and 5.2 ×/÷ 1.75 for controls. Twenty-four-hour AMBP (mean systolic/diastolic mm Hg ± SD) was significantly higher in micro. (131 ± 10/78 ± 7) than in normo. (122 ± 8/73 ± 6; $P < 0.001/P < 0.01$). No 24-hour AMBP difference between normo. and controls (120 ± 9/71 ± 7) was found. No difference in the night/day ratio of blood pressure was found between the diabetic groups. Coefficient of variation for day time systolic measurements did not show any intergroup difference. Systolic day time blood pressure for the pooled diabetic group correlated significantly with UAE ($r = 0.45$, $P < 0.001$), whereas no significant correlation with auscultatory systolic values in the clinic was found ($r = 0.21$; $P = 0.09$). In conclusion, blood pressure in micro. as compared to normo. is not more labile but is elevated day and night without significant alteration of the diurnal rhythm. AMBP reflects the association between UAE and blood pressure more precisely than clinical measurements and may be preferable for identifying candidates for antihypertensive treatment.

A number of studies [1–7] have documented an elevated office blood pressure level in microalbuminuric type 1 diabetic patients, albeit seldom to the level of frank hypertension according to WHO criteria [8]. Experiences during the last two decades in healthy individuals and patients with essential hypertension have shown that casual blood pressure is not necessarily representative of blood pressure readings throughout a 24 hour period [9]. Ambulatory blood pressure (AMBP) monitoring allows multiple indirect blood pressures to be obtained while patients are engaged in their normal activities at home or at work. Several studies in essential hypertensive subjects have uniformly found that AMBP correlates better with hypertensive organ lesions (especially left ventricular mass) than casual blood pressure [10–12], and the only prospective study published has demonstrated an improved prognostive value of AMBP with respect to cardiovascular morbidity and mortality [13, 14].

Increase in blood pressure is one of the clinical hallmarks of diabetic nephropathy [15, 16] and early antihypertensive therapy has improved life expectancy in overt nephropathy dramatically [17]. Blood pressure starts to increase in close relationship to development of persistent microalbuminuria [18], and a significant correlation exists between annual rate of increase in urinary albumin excretion (UAE) and blood pressure [5, 19]. Furthermore, intervention studies with antihypertensive therapy in microalbuminuric patients have demonstrated the ability to arrest or reverse the natural course of increasing UAE [20–22].

Refined techniques for research or clinical use have been introduced to secure accurate determination of both kidney function and subclinical elevations of UAE. Evaluations of long-term metabolic control are no longer based on occasional measurements of blood glucose, however, the measurement of blood pressure still largely depends on casual blood pressures with well known limitations [23, 24].

The aim of this study was to characterize 24-hour ambulatory blood pressure pattern in two well-matched groups of normo- and microalbuminuric type 1 diabetic patients, respectively, and to relate this to blood pressure obtained in the clinic and to urinary albumin excretion as a possible marker of the hypertensive load on the kidneys. A group of healthy control persons was included.

Methods

Patients

Adult outpatients from several centers in Aarhus county mailed samples of three early morning urine collections to our laboratory. Microalbuminuria was suspected if urinary albumin concentration was above 20 μg/ml in more than one sample, and such patients subsequently collected three timed-overnight urines within one week. The presence of microalbuminuria was accepted if UAE was above 20 but below 200 μg/min in more than one sample.

Thirty-four microalbuminuric (micro.) patients were included in the study, and for each a normoalbuminuric (normo.) patient was matched with respect to sex, age and diabetes duration. Normoalbuminuria was defined as UAE below 20 μg/min in more than one of three overnight urine collections. Healthy controls recruited among medical students and friends of the patients were individually matched to their diabetic counterpart

Table 1. Clinical data of type 1 diabetic patients and healthy controls studied

	Micro-albuminuric	*P*	Normo-albuminuric	*P*	Controls
N	34	—	34	—	34
Sex (M/F)	24/10	—	24/10	—	24/10
Age *years*	30.1 ± 10.3 (19–49)	NS[a]	31.0 ± 10.1 (16–49)	NS[a]	30.5 ± 10.5 (18–53)
Diabetes duration *years*	17.7 ± 6.4 (8–28)	NS[b]	18.0 ± 6.9 (6–31)		
Body mass index kg/m^2	23.9 ± 2.9 (18.9–32.1)	NS[a]	23.7 ± 2.6 (19.5–32.4)	NS[a]	23.1 ± 3.2 (18.9–35.0)
HbA_{1c} %	9.1 ± 1.3 (7.2–13.5)	<0.02[b]	8.3 ± 1.5 (5.0–11.2)	—	5.1 ± 0.59 (3.6–6.2)
Serum creatinine *μmol/liter*	79 ± 13 (53–110)	NS[a]	78 ± 11 (55–100)	NS[a]	82 ± 12 (61–107)
Insulin dose *U/kg*	0.74 ± 0.24 (0.32–1.39)	NS[b]	0.68 ± 0.17 (0.43–1.05)		
Retinopathy (normal/background/proliferative)	6/23/5	<0.001[b]	23/11/0		
Smoker (yes/no)	19/15	NS[b]	13/21	NS[c]	10/24
Oral anticonception (yes/no)	1/9	NS[b]	1/9	NS[c]	3/7
Ambulatory monitoring on working day (yes/no)	8/26	NS[b]	8/26	NS[c]	10/24
Urinary albumin excretion *μg/min*	51.7×/÷1.94 (20.2–198.3)	—	5.1×/÷1.88 (1.1–13.1)	NS[c]	5.2×/÷1.75 (1.6–25.2)

Values are mean ± SD or geometric mean ×/÷ tolerance factor and (range). NS, not significant; [a] analysis of variance; [b] comparison between micro- and normoalbuminuric patients; [c] comparison between normoalbuminuric patients and controls.

for sex and age. AMBP in the micro. patient was measured on working days or days off as convenient for the patient. Normo. patients and controls were measured on the same kind of day as their micro. partner, but strict individual matching was not possible in two controls.

Inclusion criteria for patients was age <50 years and type 1 diabetes which was defined as a constant need for insulin treatment since diagnosis before the age of 35 years. Patients and controls were excluded if they had ever been treated with diuretics or antihypertensive drugs. No blind, amputated or pregnant persons were included. One normo. patient was treated with insulin pump and the rest with one or multiple daily injections. Clinical data of the patients are shown in Table 1.

All participants were given verbal as well as written instructions for correct urine sampling. Blood samples were drawn for measurement of glycosylated hemoglobin HbA_{1c} by HPLC [25], and serum creatinine (Jaffe's method). Retinopathy was assessed by funduscopy. Urinary albumin excretion was measured by radioimmunoassay [26] and overnight specimens were dipstick tested (Multistix 8SG, Ames, Stokes Court, UK) to secure nonketonuria and the absence of positive nitrite or leukocytesterase reaction.

The study was approved by the local ethical committee and all participants gave their informed consent.

Equipment for blood pressure monitoring

Ambulatory blood pressure was measured by means of a lightweight (660 g) portable automatic monitor, SpaceLabs model 90202 (Redmond, Washington, USA) using oscillometry [27]. The monitor was programmed to cuff insufflations every 20 minutes from 6 a.m. to midnight and every hour during the night.

After demonstration of the equipment and performance of two measurements for habituation, three oscillometric and three auscultatory blood pressures were measured on the same arm while the patient was sitting. The averages of these three values were named the clinic oscillometric and the clinic auscultatory blood pressures. All auscultatory measurements were performed by the same investigator using a random zero sphygmomanometer (Hawskley and Sons, Lancing, UK) taking Korotkoff V as diastolic value. If upper arm circumference exceeded 35 cm (one case) the normal size cuff (12 × 22.5 cm) was exchanged with a large cuff (15.5 × 38 cm). Oscillometric measurements were performed with normal and obese arm cuffs specially designed by the manufacturer.

The patients were asked to note time for going to bed and rising in the morning and this information was used for calculating day- and nighttime AMBP as the hourly mean values in the respective period. The patients were instructed to keep the arm perfectly still in the phase of deflation, as the equipment is extremely sensitive to movement in this period; otherwise we did not attempt to make any standardization with respect to physical activity. Unclear transducing of signals, mostly because of arm movements, automatically triggered a remeasurement within two minutes.

Automatic computerized editing of the 24-hour blood pressure report was performed in order to reject readings that most likely were erroneous. The following criteria were used: systolic blood pressure >260 or <70 mm Hg, diastolic blood pressure >150 or <40 mm Hg and heart rate >200 or <20 beats/min.

Statistical analysis

Parametric statistical analysis was performed whenever possible. Urinary albumin excretion was logarithmically transformed before any statistical analysis and variability was expressed as geometric mean ×/÷ tolerance factor (antilog of

Table 2. Clinic and ambulatory blood pressure (oscillometry) in type 1 diabetic patients and healthy controls

	Micro-albuminuric	*P*	Normo-albuminuric	*P*	Controls
Systolic clinic BP *mm Hg*	131.6 ± 9.1	NS[b]	127.6 ± 11.6	NS[c]	124.6 ± 9.8
Systolic day time BP *mm Hg*	135.9 ± 9.6	<0.001[b]	127.2 ± 9.4	NS[c]	124.9 ± 9.4
Systolic night time BP *mm Hg*	122.2 ± 11.4	<0.0001[b]	112.0 ± 7.6	NS[c]	108.6 ± 9.4
Systolic 24 hr BP *mm Hg*	131.3 ± 9.6	<0.001[b]	122.4 ± 8.2	NS[c]	119.2 ± 9.1
Systolic night/day ratio	0.90 ± 0.06	NS[a]	0.88 ± 0.06	NS[a]	0.87 ± 0.05
Diastolic clinic BP *mm Hg*	78.6 ± 7.4	<0.05[b]	74.4 ± 8.1	NS[c]	73.5 ± 7.7
Diastolic daytime BP *mm Hg*	81.6 ± 7.0	<0.01[b]	77.0 ± 7.0	NS[c]	76.5 ± 7.2
Diastolic nightime BP *mm Hg*	69.1 ± 8.2	<0.001[b]	62.6 ± 6.6	NS[c]	60.7 ± 7.5
Diastolic 24 hr BP *mm Hg*	77.5 ± 7.2	<0.01[b]	72.5 ± 6.1	NS[c]	71.0 ± 7.0
Diastolic night/day ratio	0.85 ± 0.07	NS[b]	0.82 ± 0.08	NS[c]	0.80 ± 0.07

Values are mean ± SD, $N = 34$ in each group. NS, not significant; [a] analysis of variance; [b] comparison between micro- and normoalbuminuric patients; [c] comparison between normoalbuminuric patients and controls.

arithmetic mean and of standard deviation of log transformed data, respectively). Differences between groups were assessed by an unpaired *t*-test only if analysis of variance indicated significant differences. In cases of nonhomogenity of variance (Bartlett's test), Kruskall-Wallis test was used and in cases of significance followed by a Mann-Whitney test. Data within groups were compared by a paired *t*-test. Fischers exact test was used for noncontinuous variables and McNemars test for paired data. Correlations were calculated as the product-moment correlation coefficient *r*. Multiple stepwise regression analysis was accomplished as a forward selection procedure. $P < 0.05$ (two-tailed) was accepted as level of statistical significance. All statistical analysis was done by the commercial available program Statgraphics (STSC, Rockville, Maryland, USA).

Results

Apart from matching parameters micro. and normo. patients were compatible with regard to body mass index, insulin dose, serum creatinine and smoking status. Normo. patients were comparable to controls also with respect to UAE. HbA_{1c} was significantly higher in micro. (9.1 ± 1.3%) than in normo. patients (8.2 ± 1.5%; $P < 0.02$), and retinopathy was more frequent in micro. patients ($P < 0.001$).

Auscultatory clinic blood pressure did not differ significantly between groups. Systolic auscultatory values were: micro. 124 ± 12.0 mm Hg, normo. 120.8 ± 13.5 mm Hg and controls 118.7 ± 10.6 mm Hg. However, a tendency towards higher diastolic auscultatory blood pressure in micro. (81.0 ± 8.8 mm Hg) compared with normo. patients (76.7 ± 9.7 mm Hg) was noted ($P = 0.057$), while no difference between normo. patients and controls (75.3 ± 8.8 mm Hg) was found. Oscillometric clinic blood pressure values are shown in Table 2.

AMBP revealed a significant elevation of 24 hour, daytime and nighttime blood pressure in micro. patients compared with the normo. group, whereas no difference could be found between normo. patients and controls (Table 2). Similar results were obtained if the comparison of AMBP was restricted to the 28 micro., 33 normo. patients and 31 controls who had an auscultatory diastolic clinical value <90 mm Hg. The 24-hour blood pressure profiles are depicted in Figures 1 and 2.

Diastolic daytime values were significantly higher than clinic blood pressures in all groups ($P < 0.05$). The night/day ratios of systolic blood pressure were comparable between groups, but

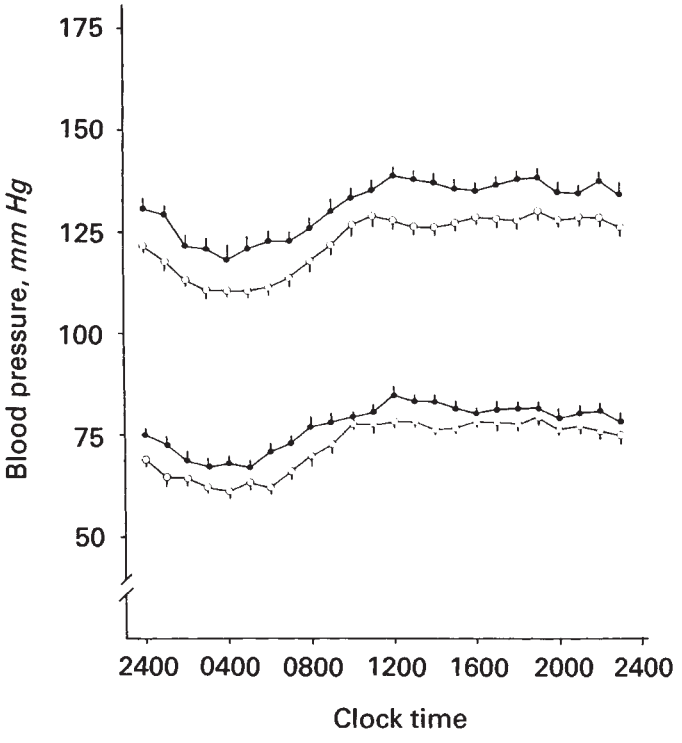

Fig. 1. *Twenty-four hour profile of hourly mean systolic and diastolic blood pressure for microalbuminuric (N = 34, filled circles) and normoalbuminuric (N = 34, open circles) type 1 diabetic patients.* Vertical bars represent standard errors.

significant intergroup differences in diastolic ratio could be demonstrated by analysis of variance ($P < 0.02$). The night/day ratio of diastolic blood pressure in micro. was 0.85 ± 0.07, which was not significantly different from normo. patients: (0.82 ± 0.08, $P = 0.09$). The 95% confidence interval for the difference in ratios (micro.-normo.) was from −0.005 to 0.069.

Variability of blood pressure was evaluated as the coefficient of variation for all systolic measurements in the period (6.00 to 23.00). Values were 9.5 ± 1.8 for micro. 9.2 ± 2.2 for normo. patients and 9.4 ± 1.8 for controls, without intergroup difference.

The clinical usefulness of AMBP was also assessed by plotting daytime diastolic values against clinic oscillometric

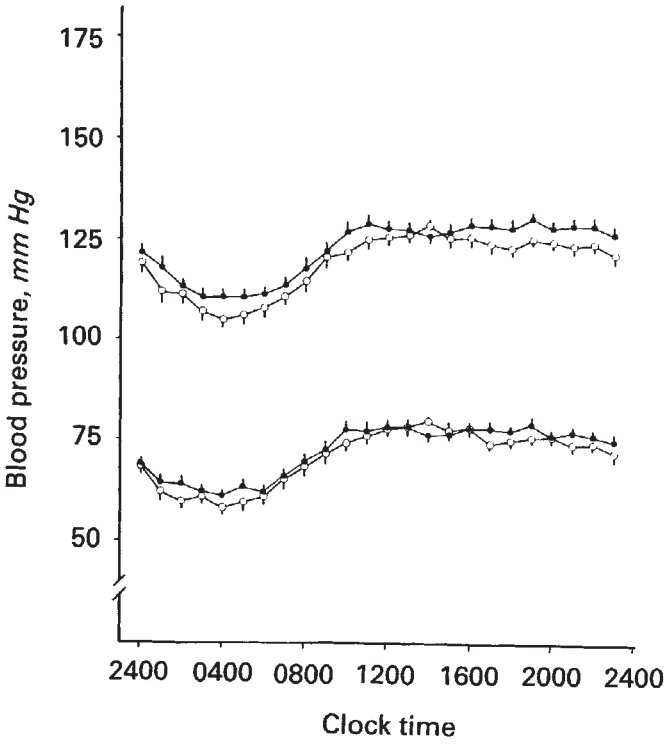

Fig. 2. *Twenty-four hour profile of hourly mean systolic and diastolic blood pressure for normoalbuminuric type diabetic patients* (N = *34, filled circles) and healthy controls* (N = *34, open circles).* Vertical bars represent standard errors.

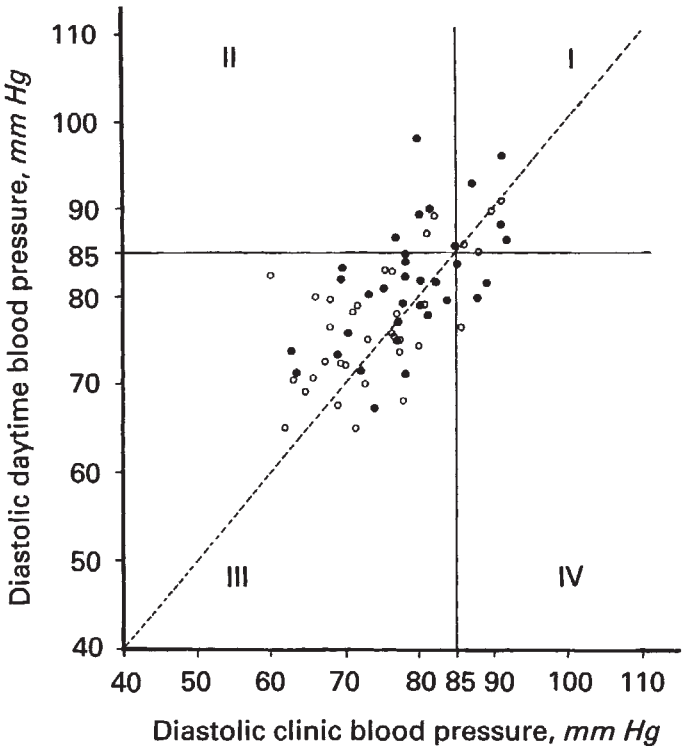

Fig. 3. *Diastolic daytime blood pressure plotted against clinic oscillometric blood pressure for microalbuminuric* (N = *34, filled circles) and normoalbuminuric* (N = *34, open circles).*

values (Fig. 3). Seven patients (10%) had an oscillometric diastolic value below 85 mm Hg, but a daytime average above 85 mm Hg (quadrant II); whereas the opposite situation was present for three patients (quadrant IV; NS).

The prevalence of measurements in the period 6.00 to 23.00 which was above 140 mm Hg systolic or 90 mm Hg diastolic was assessed. No difference was found between normo. and controls whereas the prevalence of hypertensive measurements in micro. significantly outranged that for normo. patients (Table 3).

Ambulatory blood pressure as related to urinary albumin excretion

Systolic blood pressures (day, night and 24 hour) correlated significantly with UAE in the pooled diabetic group; the correlation coefficient was 0.45 for daytime values ($P < 0.001$) and 0.53 for night values ($P < 0.0001$). In contrast, no significant correlation was found between auscultatory blood pressure and UAE ($r = 0.21$, $P = 0.09$; Fig. 4). Ambulatory diastolic blood pressures also correlated with UAE in the combined diabetic group, but with lower r values (data not shown). In the groups analyzed separately the only significant correlation found was between UAE and night blood pressure in normo. patients (systolic $r = 0.40$, $P < 0.05$).

Also HbA_{1c} and UAE correlated among all diabetic patients ($r = 0.36$, $P < 0.01$), but not in subgroups of diabetes.

The multiple stepwise selection was performed in the pooled diabetic group selecting among the following independent variables: age, diabetes duration, body mass index, HbA_{1c}, sex, smoking, and UAE. The determinants selected are mentioned in order of significance. With systolic 24-hour blood pressure as the dependent variable, UAE and sex were identified as the only independent determinants ($R^2 = 0.27$, $P < 0.0001$ analysis of variance for the full regression). The only correlates to diastolic 24-hour blood pressure were UAE and diabetes duration ($R^2 = 0.24$, $P < 0.001$). Correlates with diastolic night blood pressure in the combined diabetic group were UAE, age and HbA_{1c} ($R^2 = 0.43$, $P < 0.0001$), whereas HbA_{1c} was the only correlate in the micro. group analyzed separately ($R^2 = 0.23$, $P < 0.01$).

Multiple stepwise selection was also performed in the pooled diabetic group with UAE as the dependent variable. In addition to systolic and diastolic night blood pressure, the possible independent variables included are listed above. As UAE was based on overnight samples, only nighttime blood pressures were assessed as a possible correlate. The night time systolic blood pressure was the only factor selected as an independent determinant ($R^2 = 0.27$, $P < 0.0001$).

Ambulatory blood pressure as related to HbA_{1c}

Diastolic and systolic nighttime blood pressure correlated significantly with HbA_{1c} in diabetic patients ($r = 0.42$, $P < 0.001$ and $r = 0.31$ $P < 0.01$). In diabetic subgroups diastolic night blood pressure was still clearly correlated to HbA_{1c} ($r = 0.51$, $P < 0.01$) in micro. but not in normo. patients.

Table 3. Frequency of daytime (6.00–23.00) blood pressures in the hypertensive range

	Micro-albuminuric	*P*	Normo-albuminuric	*P*	Controls
Systolic BP >140 mm Hg %	28 (4–90)	<0.001[b]	13 (0–7)	NS[c]	4 (0–58)
Diastolic BP >90 mm Hg %	16 (0–75)	<0.05[b]	4 (0–57)	NS[c]	4 (0–55)

Values are median (and range). NS, not significant; [b] comparison between micro- and normoalbuminuric patients; [c] comparison between normoalbuminuric patients and controls.

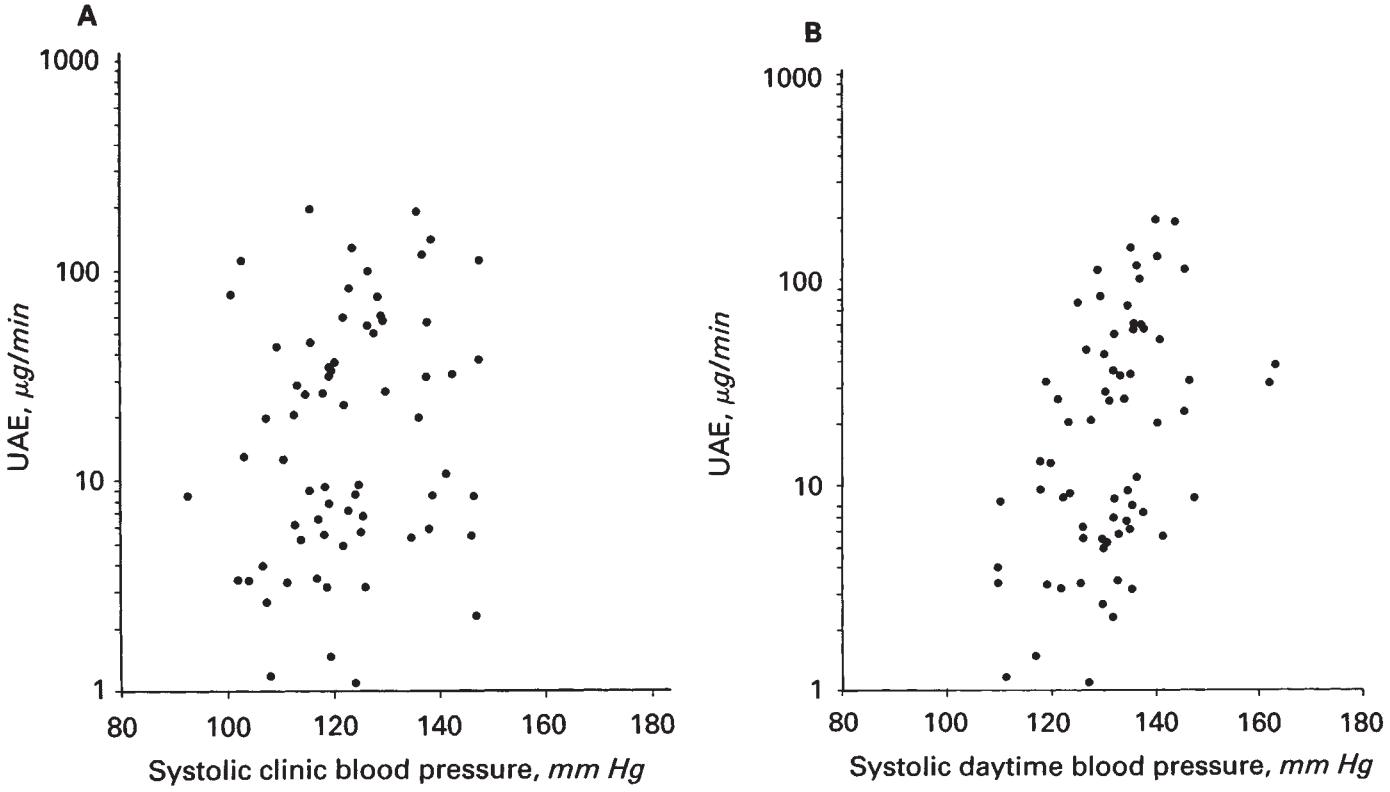

Fig. 4. *Correlation between UAE (log scale) and* (**A**) *systolic clinic blood pressure measured by sphygmomanometry (r = 0.21,* P = *0.09) and* (**B**) *systolic day time value (r = 0.45,* P < *0.001) in type 1 diabetic patients* (N = *68).*

Heart rate

The daytime mean heart rate in micro. patients was significantly higher than in normo. patients (88.0 ± 10.0 vs. 82.6 ± 10.1, $P < 0.05$) and the heart rate in normo. patients was higher than in controls (75.8 ± 11.1, $P < 0.05$; Fig. 5). No difference between micro. (69.1 ± 11.1) and normo. patients (67.1 ± 11.3) could be found for the heart rate during the night but night heart rate was higher for normo. patients than controls (59.6 ± 10.2, $P < 0.01$). The heart rate decreased about 20% at night with no intergroup differences.

Calibration

We found a significant difference between the two techniques for both systolic ($P < 1 \cdot 10^{-10}$) and diastolic blood pressures ($P < 0.01$; $N = 102$). The mean systolic difference (oscillometric − auscultatory) was 6.5 ± 5.9 mm Hg and the mean diastolic difference was −2.1 ± 7.0 mm Hg. The same results were obtained if the calibration was evaluated in the group of controls only.

Discussion

In contrast to previous results, we did not find that blood pressure was statistically significantly elevated in micro. patients when measured in the clinic by sphygmomanometry. The blood pressures in the micro. group in our study, encompassing only patients without antihypertensive treatment, was considerably lower than previously found, probably reflecting the recent change in attitude towards early initiation of antihypertensive medication in such patients (Table 4). The use of Hawskleys random zero sphygmomanometer, necessary to blind the observer who was aware of the UAE level of the patients, could contribute as an explanation since this device has been reported to underestimate blood pressure compared to ordinary sphygmomanometers [28]. It is still a controversy whether this underestimation is true or reflects the improved capability of unprejudiced measurements to recognize the well known decrement in blood pressure by repeated measurements on the same occasion in the same patient [29]. The higher ambulatory 24-hour blood pressure measurements in micro.

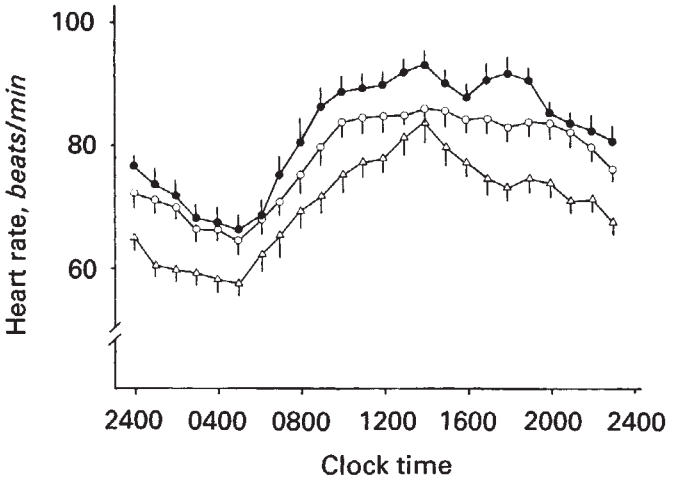

Fig. 5. *Twenty-four-hour profile of mean hourly heart rate in microalbuminuric (N = 34, filled circles), normoalbuminuric (N = 34, open circles) type 1 diabetic patients and healthy controls (N = 34, open triangles).* Vertical bars represent standard errors.

Table 4. The changing level of blood pressure in microalbuminuric diabetic patients

	Year of publication	Number	Mean age *years*	Blood pressure *Mean syst/diast*[a] *mm Hg*
Mogensen & Christensen [1]	1984	12	35	138/92
Wiseman et al [2]	1984	12	34	136/87
Mathiessen et al [3]	1984	22	31	131/85
Feldt-Rasmussen et al [4]	1985	34	32	135/86
Christensen & Mogensen [5]	1985	25	27	133/88
Berglund et al [6][b]	1987	16	33	135/77
Le Floch et al [7][b]	1990	23	45	133/77
Present study	1991	34	30	124/81

[a] Clinic blood pressures by sphygmomanometry
[b] Patients defined as hypertensive excluded from these studies

compared to normo. patients were not due to selection bias as similar results were found in the subpopulation of patients who had a diastolic blood pressure below 90 mm Hg when measured in the clinic. A recent study including 25 diabetic patients with different degrees of albuminuria reported a significantly elevated ambulatory blood pressure in the diabetic group compared to a control group, but it is not possible to deduce if this increase was associated with diabetes *per se* or the presence of early renal complications in some of the patients [30]. We found no difference between AMBP in our normo. group as compared to controls, indicating that elevated AMBP in diabetic patients without overt nephropathy is a phenomenon closely related to microalbuminuria. This is in concert with findings indicating that the prevalence of hypertension is not different in normo. patients and the background population [31].

HbA_{1c} was higher in micro. patients and elevated AMBP in these patients could be a consequence of poor glycemic control rather than early renal dysfunction. This may be supported by the finding of an independent positive association between HbA_{1c} and diastolic blood pressure during the night. It can be speculated that metabolic control might influence the nocturnal level of pressor active hormones and thus contribute to the variation of blood pressure unmodulated by physical activity. However, with respect to 24-hour blood pressure, the multiple stepwise regression procedure identified UAE as a main determinant and excluded HbA_{1c} as independently influencing the variation of 24-hour blood pressure. This suggests that in a cross sectional study, glycemic control is not directly associated with 24-hour blood pressure beyond the level of an association between poor glycemic control and microalbuminuria. Short term studies have shown increased blood pressure when glycemic control deteriorates [32, 33]. The possible impact on 24 hour AMBP awaits similar intervention studies before this can safely be discussed.

Autonomic function of the diabetic patients was not assessed. The small but significant elevations of heart rate during the day in micro. compared with normo. patients as well as in normo. patients compared to controls are probably explained by autonomic dysfunction [34]. Thus dysautonomia has been already documented in early stages of diabetic renal disease [35, 36]. On the other hand, we did not recognize a significant difference between night/day ratios of blood pressure in micro. and normo. patients as would have been expected if important differences in autonomic function between the two diabetic groups were present.

A clinic diastolic blood pressure above 85 mm Hg has been proposed as a level for introducing antihypertensive therapy [37]. The main problem of relying on clinic blood pressure in this category of young and active diabetic patients seemed to be the risk of underestimating the blood pressure during normal daily activities. This is in contrast with the problem of "white coat hypertension" which is a well described phenomenon in patients with mild essential hypertension, leading to an important overdiagnosing of elevated blood pressure [38]. The reason for this discrepancy is probably that the vast majority of our patients were normotensive [39]. The frequency of measurements in the hypertensive range (the blood pressure load) has been suggested as a more precise determinator for hypertensive organ lesion than a simple daytime or 24 hour average measurement [40]. We found an increased burden of ambulatory blood pressure measurements above 90 mm Hg in micro. patients compared with normo. patients though the auscultatory values in the clinic were comparable. A logical conclusion of these findings is to recommend the performance of ambulatory blood pressure in all patient with persistent microalbuminuria.

Guidelines for institution of antihypertensive treatment cannot be given from the data found in our study. This aspect awaits results of prospective studies incorporating AMBP and long-term effects of treating normotensive micro. patients with angiotensin converting enzyme inhibitors. Meanwhile a certain level of clinic blood pressure must be accepted as an indication for initiation of antihypertensive treatment [37]. It may seem difficult to argue against initiation of treatment in micro. patients with clinic blood pressures below, but daytime averages above this level. In fact our finding of a significant correlation between UAE and daytime average blood pressure, but not clinic auscultatory blood pressure indicates that AMBP results could be a more informative parameter of the blood pressure load on the kidneys, and may serve as a guide for treatment on

a more relevant pathophysiological basis. Interestingly 'improved' correlations between blood pressure and UAE has also been found in essential hypertension with application of AMBP [41–43]. As discussed by Coats, such superior correlations could be a statistical phenomenon related to a reduced day to day variability of AMBP because of the large number of measurements [44]. The question of a possible inherent value of ambulatory measurements as correlates to UAE (and other variables like left ventricular mass) is interesting, but even if the improved correlation depends mainly on the multiplicity of measurements, such are most feasibly obtained in clinical practice by performing ambulatory rather than clinic measurements.

As UAE was assessed from overnight samples in our study it is not surprising that we found the highest correlation with night blood pressures.

Exercise test has shown an exaggerated blood pressure response in micro. patients and this has been suggested as an argument for choosing beta blockers in case of antihypertensive treatment [45]. Our study does not support the idea that daily life blood pressure in micro. patients should be more labile. We have found comparable coefficients of variation in blood pressure of the two diabetic groups. On the other hand the increased heart rate, together with other indications of a hyperkinetic cardiac function in micro. patients [46], could add to the discussion on rational adjunct drugs in favor of choosing cardioselective beta blockers [47].

The SpaceLabs 90202 monitor is one of the presently available devices which has proved to fulfill the standards of the American Association for the Advancement of Medical Instruments (AAMI) [27] and has confidently been recommended for clinical use [48]. Nevertheless, in the range of blood pressures in this study, we found a significant overestimating of the systolic blood pressure and underestimating of the diastolic blood pressure. This does not affect the comparison between groups with the same range of blood pressures, but our findings stress the importance of individual calibration [49].

We have previously found a higher reproducibility of 24-hour blood pressure compared with clinic measurements [50], suggesting that intraindividual changes in blood pressure during time can be precisely evaluated by AMBP. The optimal parameter for monitoring blood pressure in patients at risk for developing nephropathy may be the individual AMBP changes over years, combined with changes in UAE, rather than measurement of clinic blood pressure.

Acknowledgments

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